www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v7i3.54

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Association of Vitamin D levels with the severity of bronchial asthma in adult patients

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Abstract
Introduction: *Role of diet in causation and exacerbation of asthma has been proposed by numerous authors, of which the role of vitamin D status is of particular interest. The present study is aimed to assess the association of vitamin D levels with the severity of bronchial asthma.*
Methodology: *This cross-sectional study was conducted in the Department of General Medicine, DY Patil School of Medicine, Navi Mumbai in which 90 asthmatic patients were included. Using a pre-designed semi-structured questionnaire, demographic and clinical information of the patients was obtained. Biochemical variables like serum calcium, phosphate, alkaline phosphatase and vitamin D levels were noted. Mean vitamin D levels of patients with mild, moderate and severe asthma were compared.*
Results: *The baseline demographic data of the patients like age and gender distribution was similar in the three asthmatic groups. Serum 25-OH-cholicalciferol levels were significantly lower (p value <0.01) among patients with severe asthma. Vitamin D deficiency (<20 ng/ml) was observed in a total of 30 patients, insufficiency (20 to 29 ng/ml) in 44 patients and sufficiency (30 to 100 ng/ml) in 16 patients. Vitamin D levels were found to be significantly associated with the severity of asthma (p value < 0.001).*
Conclusions: *The appropriate dose, route, and safety of vitamin D supplementation in asthmatics needs to be established. Molecular studies of vitamin D receptors to explain the role of vitamin D supplementation in asthma are needed in future.*
Keywords: *Asthma severity; Bronchial asthma; Vitamin D deficiency; Vitamin D insufficiency.*

Introduction

Asthma, a prolonged inflammatory disorder with hyper responsiveness of the airways, is one of the most common chronic diseases worldwide, affecting approximately 300 million people.[1] Airway injury is promoted by the complex interaction between cells and inflammatory mediators, which impairs the immunogenic tolerance and result in airway remodeling.[2] Hypertrophy of smooth muscle, hyperplasia of epithelial goblet cell, and deposition of airway extracellular matrix proteins are the main

characteristics of the remodelling, which may lead to increase airflow obstruction and finally causing the respiratory symptoms. Role of diet in causation and exacerbation of asthma has been proposed by numerous authors.[3] Of these, the role of vitamin D status in airway health and homeostasis, and the effect of vitamin D deficiency on airways pathologyis of particular interest. Vitamin D is a fat-soluble vitamin which is a modulator of calcium absorption and bone health and plays an important role in immune regulation and in respiratory infections.[4] Serum 25(OH) cholecalciferol is the most commonly used indicator for overall vitamin D status since it reflects the intake of vitamin D from dietary sources intake as well as sun exposure and also accounts for the adaptation of vitamin D from adipose stores in the liver. Epidemiological research has suggested a strong, significant association between asthma pathology and reduced levels of vitamin D. However, temporality of this association has not been established so far; whether bronchial asthma pathology results in decreased vitamin D levels or low vitamin D levels cause and exacerbate bronchial asthma. The present study is aimed to assess the association of vitamin D levels with the severity of bronchial asthma.

Methodology

Study Design and Sampling

This cross-sectional study was conducted in the Department of General Medicine, DY Patil School of Medicine, Navi Mumbai in which 90 asthmatic patients were included. Patients aged 18 years or above referred or diagnosed with bronchial asthma at our outpatient clinic were included in the study. We excluded patients aged 70 years or above, with a history of major illness like liver, renal or lung diseases, those taking vitamin supplements or calcium or on anticonvulsants. The patients were explained the purpose of the study and an informed written consent was obtained from them. The study was approved by the institutional ethics committee.

Data Collection and Data Analysis

Using a pre-designed and pre-tested semi-structured questionnaire, demographic information of the patients was obtained. Anthropometric data were collected and body mass index was calculated for all patients. Clinical history was obtained and mean age at onset of asthma and mean age at diagnosis of asthma was noted for all patients. Clinical parameters of asthma severity and control measurements were done according to the criteria of Global Strategy for Asthma Management and Prevention of the Global Initiative for Asthma (GINA).[5] Based on the symptoms and therapy, patients were classified as mild, moderate and severe. Airway limitation was assessed by peak flow meter. Biochemical variables like serum calcium, phosphate, alkaline phosphatase and vitamin D levels were noted. ELISA was used for measuring serum 25-OH-cholicalciferol levels with a kit having detection limit of 0 to 120 ng/ml. Interpretation of vitamin D levels was based on the Endocrine Society Clinical Practice Guideline, which suggested a higher target level of at least 30 ng/ml.[6] The data were codified and analysed in the SPSS version 21 (IBM Copr, NY). Quantitative data were described as mean and standard deviation and qualitative data were described as frequency and percentage. Mean vitamin D levels of the three patient groups (mild, moderate and severe) were compared using the one-way ANOVA. Qualitative data were analysed using the chi-squared or Fisher's exact test. A probability value of less than 0.05 was taken as statistically significant.

Results

In the present study, we included 90 asthmatics of which 35 were classified as mild, 38 were classified as moderate and 17 were classified as severe. The baseline demographic data of the patients like age and gender distribution was similar in the three asthmatic groups (Table 1). Further the mean body mass index of the patients in the three groups was also similar. Mean of onset of asthma was 34.14 ± 1.81, 35.29 ± 2.54

and 37.51 ± 2.17 years for patients with mild, moderate and severe asthma respectively and mean age of diagnosis for the patient group was 34.98 ± 1.92, 38.10 ± 1.74 and 38.65 ± 1.99 years respectively. Table 2 compares the biochemical variables among the three asthmatic groups. Mean serum calcium was significantly different between the three patient groups and was found to be lower in patients with severe asthma (p value = 0.02). Serum phosphorus levels were significantly different between the three patient groups as well (p value <0.001). Serum alkaline phosphatase levels were significantly higher (p value <0.01) and serum 25-OH-cholicalciferol levels were significantly lower (p value <0.01) among patients with severe asthma. Vitamin D deficiency (<20 ng/ml) was observed in a total of 30 patients, insufficiency (20 to 29 ng/ml) in 44 patients and sufficiency (30 to 100 ng/ml) in 16 patients. Table 3 describes the distribution of patients with asthma according to their Vitamin D levels and severity of asthma and the association was found to be statistically significant (p value < 0.001). We found a significantly higher proportion of Vitamin D deficient patients with severe asthma.

Table 1 Distribution of patients according to their baseline characteristics

	Severity of asthma		
	Mild (n=35)	Moderate (n=38)	Severe (n=17)
Mean age (in years)	39.4 ± 7.9	40.2 ± 10.1	39.8 ± 11.4
Gender distribution			
Females	21 (60%)	23 (60%)	11 (65%)
Males	14 (40%)	15 (40%)	06 (35%)
Body mass index (kg/m^2)	24.5 ± 3.11	25.6 ± 3.08	24.9 ± 3.7
Mean age at onset of asthma (in years)	34.14 ± 1.81	35.29 ± 2.54	37.51 ± 2.17
Mean age at diagnosis of asthma (in years)	34.98 ± 1.92	38.10 ± 1.74	38.65 ± 1.99

Table 2 Comparison of biochemical variables among the patient groups

	Severity of asthma			P value
	Mild (n=35)	Moderate (n=38)	Severe (n=17)	
Serum calcium (mg/dl)	9.78 ± 0.61	9.66 ± 0.54	9.24 ± 0.92	0.02
Serum phosphorus (mg/dl)	5.03 ± 0.22	5.27 ± 0.31	5.10 ± 0.28	<0.001
Serum alkaline phosphatase (U/L)	233.97 ± 3.89	240.86 ± 4.22	243.12 ± 4.89	<0.01
Serum 25-OH-cholicalciferol (ng/ml)	19.88 ± 1.82	17.34 ± 1.21	13.84 ± 1.55	<0.01

Table 3 Distribution of study patients according to their vitamin D levels

Vitamin D levels	Severity of asthma		
	Mild (n=35)	Moderate (n=38)	Severe (n=17)
Deficiency (<20ng/ml)	04 (13%)	14 (37%)	12 (71%)
Insufficiency (20-29 ng/ml)	15 (41%)	24 (63%)	05 (29%)
Sufficiency (30 to 100 ng/ml)	16 (46%)	00 (00)	00 (00)
P value <0.001			

Discussion

The present study was conducted to know the association of vitamin D deficiency with bronchial asthma. We observed that the serum vitamin D levels were significantly lower in patients with moderate bronchial asthma. Also the none of the patients with severe and moderate bronchial asthma had sufficient vitamin D levels. The literature reports varied results about the association of vitamin D and development of bronchial asthma. The prevalence of vitamin D deficiency in Italian asthmatic children was found to be 53%.[7] Similar association between vitamin D levels and severity of asthma was found in another study, in which vitamin D levels were positively correlated with lung functions.[8] However, a Danish study demonstrated that vitamin D levels had no effect on the development of asthma.[9]

The role of vitamin D in asthma is not completely understood. The underlying pathology of asthmatic immune responseis airway narrowing. Over the short-term, this is due to smoothmuscle constriction and mucus secretion, while over the longer-term airway remodelling and fibrosis occur. Gupta et aldemonstrated airway smooth muscle volume fraction in endobronchialbiopsies, which was found to correlate negatively with serum vitamin D concentrations in steroid-refractory paediatric asthmatic patients.[10] This was later supported by Banerjee et al, who demonstrated that vitamin D acts on airway smooth muscle including inhibiting airway smooth muscle cell proliferation.[11] Studies have suggested that decreased level of vitamin D is correlated with an increased prevalence, hospitalization, and increased emergency visits along with declined lung function and increased airway hyper- responsiveness in asthmatic children.[12] Recently conducted clinical trials have shown the protective influence of vitamin D supplementation among asthmatic patients.[13] Moreover, increased intake of vitamin D during pregnancy has been shown to have an influence on asthma in children and adults. Gale et aldemonstrated that children whose mothers had serum 25(OH)D concentrations above 75 nmol/L had five times more risk of developing asthma at 9 years.[14] Studies from Finland and Japan found that dietary vitamin D intake during pregnancy is inversely related to the incidence of wheeze among children.[15] In contrast, another study concluded that vitamin D levels during late pregnancy were not related with the risk of childhood asthma.[16]

In addition to its role in the development of asthma, Vitamin D also has a role in asthma exacerbation. A cross-sectional study of children aged between 6 and 14 years reported that vitamin D deficiency/insufficiency was prevalent in 28% of the children and increased levels of vitamin D were associated with reduction in asthma exacerbations and reduced visits to emergency department (OR: 0.05; 95% CI: 0.004-0.71)[18] Furthermore, Brehm et al confirmed that children with vitamin D less than 30 ng/mL had increased risk of asthma exacerbations (OR: 1.5; 95% CI: 1.1-1.9).[18]

Conclusion

Supplementing vitamin D in asthmatic patients has been shown to be beneficial. However, the temporality of this observation still needs to be established. For this, clinical trials with large sample size and long follow up period are required. The appropriate dose, route, and safety of vitamin D supplementation in asthmatics needs to be established as well. Although the current evidence does not suggest screening asthmatic patients for vitamin D deficiency, but this can be explored in future studies. Also, molecular studies of vitamin D receptors to explain the role of vitamin D supplementation in asthma are needed in future.

Study Funding: None
Conflict of interest: None

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